

What is claimed is:

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5 1. A method for stimulating proliferation of endothelial or mesodermal cells, comprising the step of exposing said endothelial cells to an effective endothelial or mesodermal cell proliferation stimulating amount of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

10 1 ~~2~~. A method for activation of VEGF receptor 2, comprising the step of exposing cells bearing said receptor to an effective receptor activating dose of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

15 2 ~~3~~. A method according to claim 1, wherein said method is carried out *in vivo*.

20 3 ~~4~~. A method according to claim 1, wherein said method is carried out *in vitro*.

25 6 ~~5~~. A method for specific activation of VEGF receptor ~~2~~ comprising the step of exposing cells bearing said receptor to an effective receptor activating dose of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

7 ~~6~~. A method according to claim 6, wherein the VEGF receptor 1 is not activated.

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30 7. A method for modulating vascular permeability, comprising the step of administering an effective vascular permeability modulating amount of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

8. A method for treatment of pustular dermatitis, comprising the step of administering a therapeutically effective amount of an antagonist to a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

9. A method for treatment of pustular dermatitis, comprising the step of administering a therapeutically effective amount of an antagonist to the VEGF receptor 2.

10. A method for treatment of fluid accumulation caused by viral infection, comprising the step of administering a therapeutically effective amount of an antagonist to a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

11. A method of claim 10, wherein the viral infection is caused by an orf virus.

12. A method of claim 11, wherein said orf virus is a NZ2 strain.

13. A method of claim 11, wherein said orf virus is a NZ10 strain.

14. A host cell transformed or transfected with a vector comprising a nucleic acid sequence which encodes a polypeptide which has the property of promoting proliferation of endothelial cells, said nucleic acid consisting of the sequence of Figure 8 (SEQ ID NO:1) or of the sequence of Figure 10 (SEQ ID NO:10) and nucleic acids which hybridize under stringent conditions with said sequence, which said sequence is operably linked to a promoter sequence.

15. A host cell according to claim 14, wherein said host cell expresses a polypeptide having the property of promoting proliferation of endothelial cells by binding specifically to a VEGF receptor-2.

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16. A host cell according to claim 14, wherein said host cell is a eukaryotic cell.

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17. A host cell according to claim 14, wherein said host cell is a COS cell.

18. A host cell according to claim 14, wherein said host cell is a 293EBNA cell.

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19. A host cell according to claim 14, wherein said host cell is a prokaryotic cell.

20. A host cell according to claim 14, wherein said host cell is an insect cell.

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21. A diagnostic test kit for orf viral infection in sheep, goats and humans comprising a specific binding reagent for a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10 and means for detecting binding to said reagent.

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22. An isolated polypeptide dimer comprising a polypeptide according to Figure 9 (SEQ ID NO:2) or to Figure 11 (SEQ ID NO:2).

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23. An isolated polypeptide dimer according to claim 22, wherein said polypeptide dimer is a homodimer of said polypeptide.

24. An isolated polypeptide dimer according to claim 22, wherein said polypeptide dimer is a heterodimer of said polypeptide and at least one further growth factor selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, PlGF, NZ10 and ORFV2-VEGF.

25. An isolated polypeptide dimer according to claim 22, wherein said polypeptide dimer is a disulfide-linked dimer.

26. A pharmaceutical composition comprising an effective endothelial cell proliferation promoting amount of a polypeptide according to Figure 9 (SEQ ID NO:2) or according to Figure 11 (SEQ ID NO:11), and at least one further growth factor selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, PlGF, NZ10 and ORFV2-VEGF.

27. A pharmaceutical composition according to claim 26, further comprising heparin.

28. A pharmaceutical composition comprising an effective endothelial or mesodermal cell proliferation promoting amount of polypeptide according to Figure 9 (SEQ ID NO:2) or according to Figure 11 (SEQ ID NO:11), and at least one pharmaceutical carrier or diluent.

29. An orf VEGF-like polypeptide antagonist having the capacity to inhibit the action of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

30. An orf VEGF-like polypeptide antagonist according to claim 29, wherein said antagonist is an antibody specifically reactive with a polypeptide according to amino acid sequence of Figure 9 (SEQ ID NO:2).

31. An orf VEGF-like polypeptide antagonist according to claim 29, wherein said antagonist is an antibody specifically reactive with a polypeptide according to amino acid sequence of Figure 11 (SEQ ID NO:11).

32. An antibody according to claim 30, wherein said antibody is a polyclonal antibody.

33. An antibody according to claim 30, wherein said antibody is a monoclonal antibody.

32. An antibody according to claim 31, wherein said antibody is a polyclonal antibody.

34. An antibody according to claim 31, wherein said antibody is a monoclonal antibody.

35. An antibody according to claim 30, wherein said antibody is labeled with a detectable label.

36. An antibody according to claim 31, wherein said antibody is labeled with a detectable label.

37. An antibody according to claim 35, wherein said detectable label is radioactive isotope.

38. A orf VEGF-like polypeptide antagonist according to claim 29, wherein said antagonist is an anti-sense nucleotide sequence complementary to at least a part of the nucleotide sequence encoding a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10 or to the promoter region of ORFV2-VEGF or of ORFV10-VEGF.

39. An orf VEGF-like polypeptide antagonist according to claim 29, wherein said antagonist is an isolated polypeptide which comprises a sequence of amino acids substantially corresponding to the amino acid sequence of Figure 9 (SEQ ID NO:2) or Figure 11 (SEQ ID NO:11), wherein said polypeptide has the ability to bind to a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10 and to prevent biological activity of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

40. An isolated polypeptide which comprises a sequence of amino acids substantially corresponding to the amino acid sequence of Figure 9 (SEQ ID NO:2) or Figure 11 (SEQ ID NO:11), wherein said polypeptide has the ability to bind to endothelial cells but is unable to induce vascular permeability.

41. An isolated ORFV2-VEGF and VEGF receptor 2 complex.

42. An isolated NZ10 and VEGF receptor 2 complex.

43. A method of making a polypeptide of Figure 9 (SEQ ID NO:2) or of Figure 11 (SEQ ID NO:11), said method comprising the steps of:

culturing a host cell transformed or transfected with a vector comprising a nucleic acid sequence encoding said polypeptide operably associated with a promoter sequence such that the nucleic acid sequence encoding said polypeptide is expressed; and

isolating said polypeptide from said host cell or from a growth medium in which said host cell is cultured.

44. An isolated nucleic acid molecule comprising a polynucleotide sequence having at least 85% identity with the sequence of Figure 10 (SEQ ID NO:10).

5 45. An isolated nucleic acid molecule which encodes a polypeptide molecule comprising an amino acid sequence having at least 85% identity with the amino acid sequence of Figure 11 (SEQ ID NO:11), or a fragment or analog thereof having the biological activity of NZ10.

10 46. A vector comprising a nucleic acid according to claim 44, which nucleic acid is operably linked with a promoter sequence. *u*

15 47. A vector comprising a nucleic acid according to claim 45, which nucleic acid is operably linked with a promoter sequence.

20 48. A method of making a vector which expresses a polypeptide comprising an amino acid sequence having at least 85% identity with the amino acid sequence of Figure 11 (SEQ ID NO:11), or fragment or analog thereof having the biological activity of NZ10, said method comprising incorporating an isolated nucleic acid according to claim 44 into said vector in operatively linked relation with a promoter.

25 49. An isolated polypeptide comprising at least 85% identity with the amino acid sequence of Figure 11 (SEQ ID NO:11), or a fragment or analog thereof having the biological activity of NZ10.

30 50. An isolated polypeptide produced by expression of a polynucleotide comprising the polynucleotide sequence having

at least 85% identity with the Figure 10 (SEQ ID NO:10), or a polynucleotide which hybridizes under stringent conditions with said DNA sequence.

5 51. A means for amplifying a polynucleotide according to claim 44 in a test sample, said means comprising at least one pair of primers complementary to a nucleic acid according to claim 44.

10 52. A method for identifying an orf VEGF-like polypeptide antagonist comprising:

 admixing a substantially purified preparation of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10 with a test agent; and

15 monitoring, by any suitable means, an inhibition in the biological activity of a polypeptide selected from the group consisting of ORFV2-VEGF and NZ10.

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